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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,453	07/18/2006	Matthew David Osborne	BJS-620-412	4519

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EXAMINER	
MARVICH, MARIA	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,453	OSBORNE ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/2/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,33-41 and 43-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16, 33-41 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *replacement 2/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to an amendment filed 10/2/09. Claims 1-16, 33-41 and 43-50 are pending in this application.

Applicants have provided a copy of a DO/EO worksheet indicating that two priority documents accompany the filing of the instant application. These documents have not been identified in the instant file. In compliance with Rule 17, a request will be made on applicants' behalf for the document to be forwarded to the USPTO

> The requirement in PCT Rule 17 for a certified copy of the foreign priority application is normally fulfilled by applicant providing a certified copy to the receiving Office or to the International Bureau or by applicant requesting the receiving Office to prepare and transmit the priority document to the International Bureau if the receiving Office issued the priority document. Pursuant to PCT Rule 17.1(a)-(b), applicant must submit the certified copy, or request the receiving Office to prepare and transmit the certified copy, within 16 months from the priority date. Where applicant has complied with PCT Rule 17, the International Bureau will forward a copy of the certified priority document to each Designated Office that has requested such document with an indication that the priority document was submitted in compliance with the rule and the date the document was received by the International Bureau. This indication may be in the form of either a cover sheet attached to the copy of the priority document or a WIPO stamp on the face of the certified copy.< The U.S. Patent and Trademark Office, as a Designated Office, will normally request the International Bureau to furnish the copy of the certified priority document upon receipt of applicant's submission under 35 U.S.C. 371 to enter

the U.S. national phase. The copy from the International Bureau is placed in the U.S. national stage file. The copy of the priority document received from the International Bureau with either of the indications above is acceptable to establish that applicant has filed a certified copy of the priority document. The examiner should acknowledge in the next Office action that the copy of the certified copy of the foreign priority document has been received in the national stage application from the International Bureau.

Information Disclosure Statement

Applicants have argued that crossing out the Search reports so that they will not appear on the face of an issued patent is not supported by past practice at the USPTO. However, prosecution in other cases does not direct how the instant case will be examined. Rather, the MPEP provides driving guidance on how to properly handle all aspects of patent examination. In this instance, first, a Search Report is not a publication. (5) "Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication.". To this end, "Information submitted to the Office that does not comply with the requirements of 37 CFR 1.97 and 37 CFR 1.98 will not be considered by the Office but will be placed in the application file. (MPEP 609)" Secondly, this practice is supported by the fact that Search Reports contain listing of references that may or may not have been considered. In this case, the references cited in the ISR and British Search Report have been submitted and as stet forth in the 1449 mailed with this action, have been considered and will appear on the face of the file.

Specification

Applicants' amendment is sufficient to overcome the objections to the specification.

Claim Objections

Claims 1 and 10 are objected to because of the following informalities: recitation in line 3 of claim 1 and 10 should be amended to recite --the myeloma cell line-- as this cell has been previously recited. It is proper when referencing previously recited limitations to use the article "the" instead of "a" which indicates a new limitation.

Articles are required prior to each of the cell lines in claim 15and 47. The article "an" in claim 16 line 2 should be amended to --the--. Similar amendment to claim 48 is required.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-11, 14-16, 33, 34, 37-41, 43 and 46-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Field et al (US 6,593,140; see entire document).

Myeloma cells were cultured *in vitro* in media lacking transferrin and tropolone (lipophilic chelator) but in the presence of 0.2 mg/l of ferric ammonium citrate in suspension

culture (see e.g. example 5, line 29-31). As depicted in figure 1, the control cultures do not contain chelators. The disclosure of Fields et al states that the cells do not survive after 48 hours. Nonetheless, the cells are cultured in media meeting the requirements of the instant claims. Furthermore, as the media requirements overlap that of the instant claims, one would expect those of Fields et al to be as successful as that of the instant claims. As evidenced by the instant specification, the concentration of 1.25 mg/L of ferric ammonium citrate is about 0.2 mg/L of iron. Hence, the iron concentration is about 0.03 mg/L. The media was serum-free see example 2.

Claims 1-7, 33-41 and 43-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorfien et al (US 20060148074; see entire document).

Myeloma cells were cultured *in vitro* in suspension culture in media lacking transferring, lipophilic chelators and nitrogen containing chelators but in the presence of ferric chloride-sodium citrate (see e.g. ¶ 0094). Iron is in the concentration of 0.28 mg/L to 11 mg/L (see e.g. ¶ 0113). As evidenced by the instant specification, the concentration of 1.25 mg/L of ferric ammonium citrate is about 0.2 mg/L of iron.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16, 33-41 and 43-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Field et al (US 6,593,140; see entire document) in view of Gorfien et al (US 20060148074; see entire document).

Applicants claim a method of culturing myeloma cells in media lacking transferring, lacking lipophilic chelators and lacking synthetic and/or lipophilic nitrogen containing chelators and in the presence of ferric ammonium citrate.

The teachings of Field and Gorfien et al are described above. Gorfien teaches media for culturing myeloma wherein the iron concentration is between 0.28 and 11 mg/L Hence, the iron concentration would be about 1.75-68.75 mg/L of ferric ammonium citrate.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use ferric ammonium citrate as taught by Field et al in the media taught by Gorfien et al because Gorfien et al teach that it is within the ordinary skill of the art to use particular levels of iron to culture myeloma cells and because Gorfien et al teach that it is within the ordinary skill of the art to use ferric ammonium citrate as a source of iron. In KSR International Co. v. Teleflex lnc., 82 USPQ2d 1385 (U.S. 2007), the Supreme Court particularly emphasized "the need for caution in granting a patent based on a combination of elements found in the prior art," (Id. At 1395) and discussed circumstances in which a patent might be determined to be obvious. Importantly, the Supreme Court reaffirmed principles based on its precedent that obviousness in part is predicated on use of particular known techniques that are recognized as part of the ordinary capabilities of one skilled in the art. In the instant case, Gorfien and Field et al are both directed at methods of culturing myeloma cells. The combination of the two represents the combination of familiar elements according to known methods is likely to be

obvious when it does no more than yield predictable results." (Id. At 1395.) Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to applicants' arguments

Applicants' arguments that the media of example 5 does not explicitly state that the media is serum free, is acknowledged. However, the specification of Fields et al is directed to generation of media that supports growth of animal cells particularly in agitated cell culture in low iron concentrations. "The animal cells which may be cultured according to the invention may be for example genetically engineered cells, lymphoid cells e.g. myeloma cells, or hybridoma or other fused cells. Particular cell types include cells of human, rat, mouse or hamster origin. The medium according to the invention is particularly suitable for use with lymphoid cells, especially myeloma cells, particularly of mouse origin, especially NS/O cells." This media is in the specification either serum free or protein free, " A mouse hybridoma cell line was subcultured in a proprietary serum-free medium containing 1 mg/l human transferrin and 0.01 mg/l ferric ammonium citrate (FIG. 3b), or a proprietary protein-free medium containing 5 μM tropolone and 0.1 mg/l ferric ammonium citrate (FIG. 3a). Agitated, sparged fed-batch fermentations of the cell line in each medium were carried out (example 2)." While the media is not explicitly cited in example 5, there is reference to use of the protein free media in example 6. An assumption can be made that the media in example 5 or example 6 will be either. Nonetheless, the cells of example 5 are grown in transferring-containing, tropolone-

containing and/or ferric ammonium citrate. In this later case, the passage within example 5 teaches that the cells did not grow past 48 hours, the claims do not limit the amount of time that the cells must be grown. Hence, the ability of the cells to grow for 48 hours in the media of Fields et al meets the minimum requirements of the claims. However, figure 2 demonstrates that without transferrin but varying concentration and growth conditions with ferric ammonium citrate there is cell growth.

Gorfien et al are also directed to methods of producing media that can support growth of cells in suspension *in vitro*. The media is chemically defined, protein free containing an iron chelate and zinc. The iron chelate replaces transferrin and the zinc compound replaces insulin. As to the nature of the iron chelate, Gorfien et al teach, transferrin was replaced with 60 μM ferric chloride/sodium citrate chelate or with 40 μM ferrous sulfate/EDTA chelate (¶ 0094), "medium may, of course, be made completely protein-free by not including transferrin and insulin in the formulation. Transferrin may be replaced by ferric citrate chelates at a concentration of about 10-100 μM (preferably FeCl.sub.3-sodium citrate chelate at about 60 μM) or ferrous sulfate chelates at a concentration of about 10-100 μM (preferably FeSO.sub.4-EDTA chelate at about 40 μM)". That there is some preference for one of the disclosed forms of ferric chelate does not exclude use of the other. In fact, figure 2 demonstrates that growth in ferric chloride sodium citrate chelate is the same as that with ferrous sulfate EDTA. Applicants argue that use of ferric chloride sodium citrate chelate is higher. However, the concentration required is 60 μM which is not occluded by the instant claims. While Gorfien et al do not teach use of ferric ammonium citrate, Fields et al teach that ferric ammonium citrate provides a viable source of iron supplement. The requirement of Gorfien et al is simply that the iron be at a

concentration of 0.28 mg/L to 11 mg/L (see e.g. ¶ 0113). That the methods of Fields et al are not robust does not occlude that the art teaches that ferric ammonium citrate is a good source of iron in media culture.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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